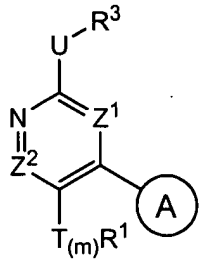
CLAIMS

We claim:

1. A compound of formula **I**:



I

or a pharmaceutically acceptable salt thereof, wherein:

Ring A is a pyrrole ring optionally substituted at the 1-position with R^z and substituted with:

(*i*) two R^y groups, and

(*ii*) QR^2;

R^z is R, C(O)R, C(O)OR, or SO_2R;

each R^y is independently selected from an optionally substituted C_{1-6} aliphatic group, Ar, CN, NO_2, halogen, $N(R)_2$, SR, or OR, provided that both R^y groups are not simultaneously Ar;

Z^1 and Z^2 are each independently selected from N or CR^x;

each R^x is independently selected from R, halogen, CN, NO_2, OR, SR, $N(R)_2$, C(O)R, or CO_2R;

U is selected from a valence bond, -O-, -S-, -N(R)-, or a C_{1-6} alkylidene chain wherein up to two methylene units of U are optionally and independently replaced by -O-, -S-, -SO-, $-SO_2-$, $-N(R)SO_2-$, $-SO_2N(R)-$, -N(R)-, -CO-, $-CO_2-$, -N(R)CO-, -N(R)C(O)O-, -N(R)CON(R)-, $-N(R)SO_2N(R)-$, -N(R)N(R)-, -C(O)N(R)-, or -OC(O)N(R)-;

T is a valence bond or a C_{1-6} alkylidene chain;

m is zero or one;

R^1 is selected from CN, halogen, OR^6, SR^6, $N(R)R^6$, or R^4;

Q is selected from a valence bond, $-C(O)N(R)-$, $-SO_2N(R)-$, $-SO_2-$, $-N(R)C(O)N(R)-$, -N(R)C(O)-, $-N(R)SO_2-$, $-N(R)SO_2N(R)-$, -N(R)C(O)O-, -C(O)-, or -C(O)O-;

R^2 is selected from halogen, CN, $(CH_2)_yR^5$, $(CH_2)_yCH(R^5)_2$, $(CH_2)_yCH(R^7)CH(R^5)_2$, $(CH_2)_yN(R^4)_2$, or $N(R^4)(CH_2)_yN(R^4)_2$;

y is 0-6;

each Ar is independently selected from an optionally substituted 3-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an optionally substituted 8-10 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

R^3 is selected from R, Ar, $(CH_2)_yCH(R^7)R^5$, CN, $(CH_2)_yCH(R^7)CH(R^5)_2$, or $(CH_2)_yCH(R^7)N(R^4)_2$;

each R is independently selected from hydrogen or an optionally substituted C_{1-6} aliphatic group, or:

two R on the same nitrogen atom are taken together with the nitrogen atom attached thereto to form a 4-8 membered saturated, partially unsaturated, or fully unsaturated ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^4 is independently selected from R^6, $C(O)R^6$, CO_2R^6, $CON(R^6)_2$, SO_2R^6;

each R^5 is independently selected from R^6, OR^6, CO_2R^6, $(CH_2)_yN(R^4)_2$, $N(R^4)_2$, $N(R)C(O)R^6$, $N(R)CON(R^6)_2$, $CON(R^6)_2$, SO_2R^6, $N(R)SO_2R^6$, $C(O)R^6$, CN, or $SO_2N(R^6)_2$;

each R^6 is independently selected from R or Ar;

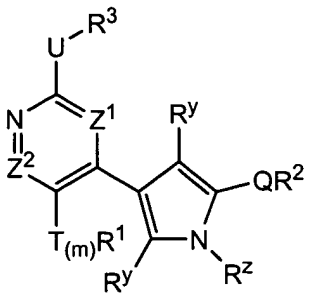
R^7 is selected from R^6, $(CH_2)_wOR^6$, $(CH_2)_wN(R^4)_2$, or $(CH_2)_wSR^6$; and

each w is independently selected from 0-4;

provided that:

when R^1 is hydrogen, U is –NH-, and R^3 is an optionally substituted phenyl ring, then Q is other than a valence bond.

2. The compound according to claim 1, wherein said compound is of formula **II**:



II

or a pharmaceutically acceptable salt thereof.

3. The compound according to claim 2, wherein:

R^1 is selected from hydrogen, $N(R^4)_2$, OR^6, 3-6 membered carbocyclyl, or an optionally substituted group selected from C_{1-6} aliphatic or a 5-6 membered aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

R^2 is selected from $(CH_2)_yR^5$, $(CH_2)_yCH(R^5)_2$, $(CH_2)_yCH(R^7)CH(R^5)_2$, or $(CH_2)_yN(R^4)_2$;

R^3 is selected from hydrogen, $CH(R^7)R^5$, 3-7 membered carbocyclyl or an optionally substituted group selected from C_{1-4} aliphatic, a 3-6 membered heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered aryl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and

U is selected from a valence bond, $-CH_2-$, -O-, -NR-, -NHCO-, or $-NHCO_2-$.

4. The compound according to claim 3, wherein R^2 is $(CH_2)_yR^5$, $(CH_2)_yCH(R^5)_2$, or $(CH_2)_yCH(R^7)CH(R^5)_2$.

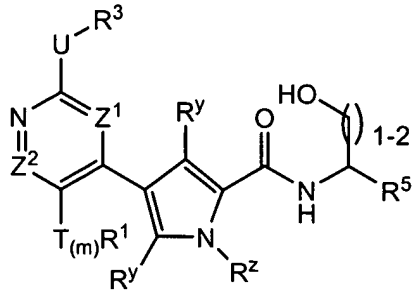
5. The compound according to claim 3, wherein Q is -C(O)N(R)- or -C(O)O-.

6. The compound according to claim 2, wherein R^3 is 3-7 membered carbocyclyl or an optionally substituted group selected from C_{1-4} aliphatic, a 3-6 membered heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered aryl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

7. The compound according to claim 2, wherein R^3 is $CH(R^7)R^5$.

8. The compound according to claim 2, wherein R^3 is a 3-6 membered heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

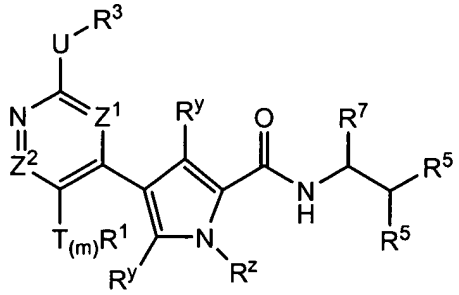
9. The compound according to claim 1, wherein said compound has the formula **III**:



III

or a pharmaceutically acceptable salt thereof.

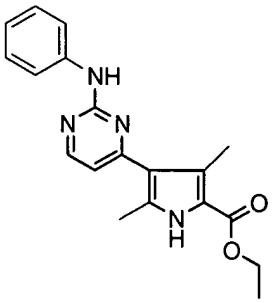
10. The compound according to claim 1, wherein said compound has the formula **IV**:



IV

or a pharmaceutically acceptable salt thereof.

11. The compound according to claim 1, wherein said compound is selected from the group consisting of:



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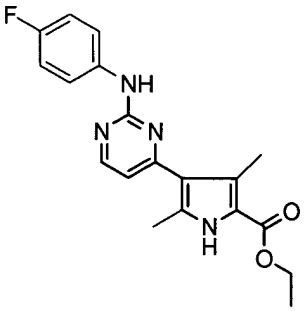

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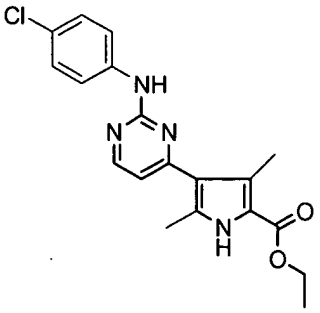

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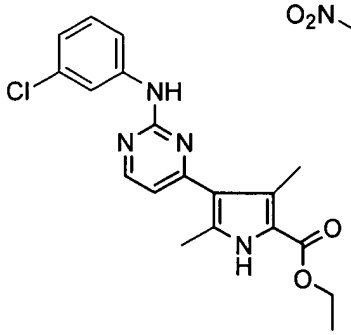

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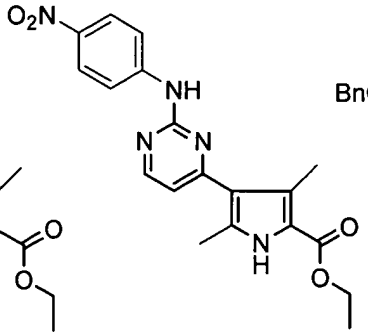

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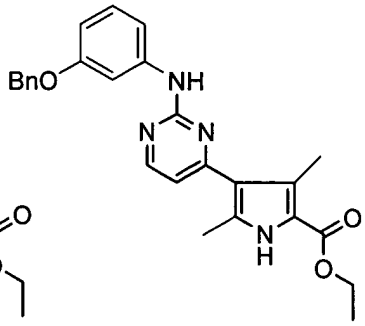

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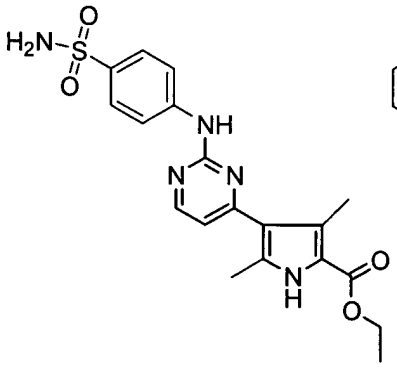

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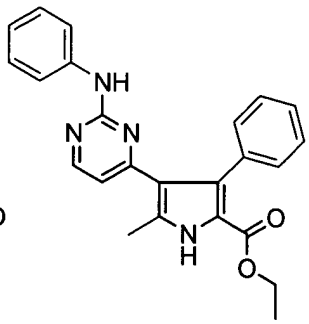

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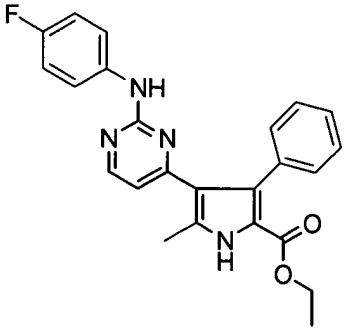

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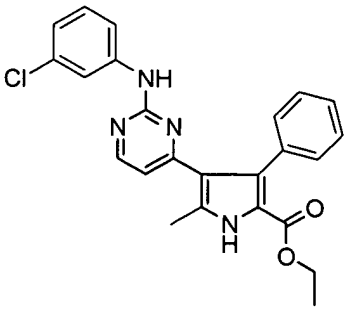

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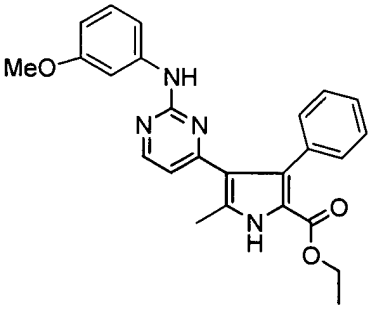

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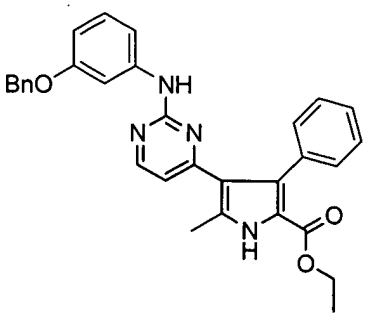

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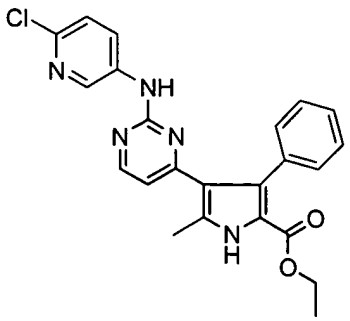

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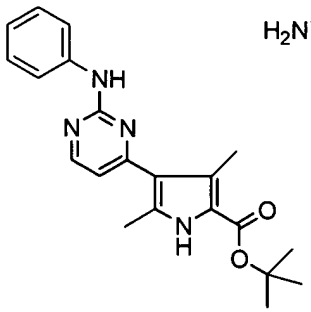

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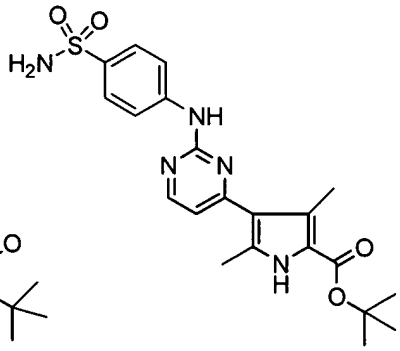

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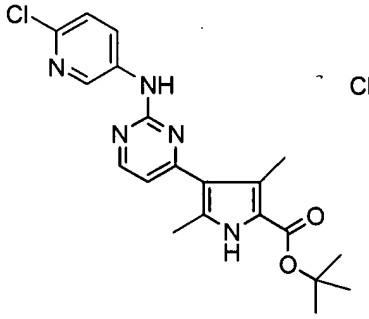

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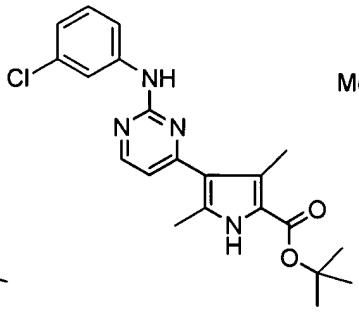

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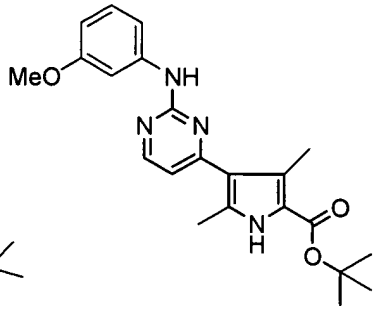

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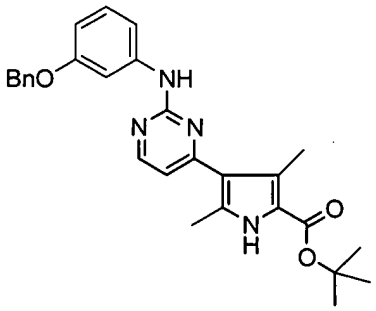

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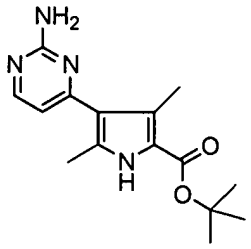

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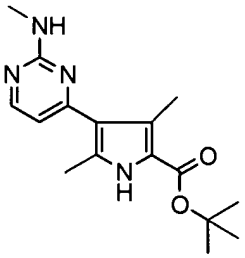

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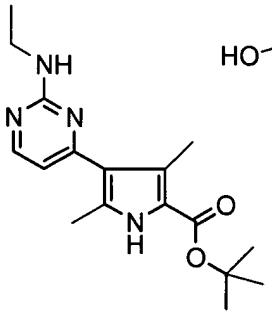

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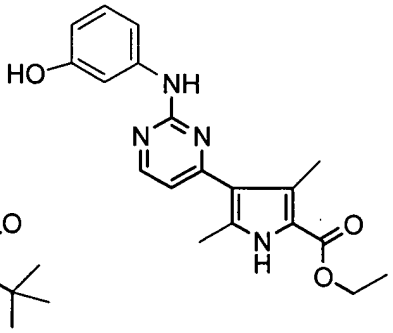

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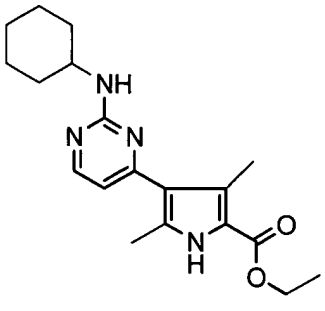

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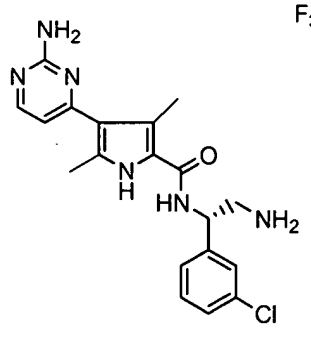

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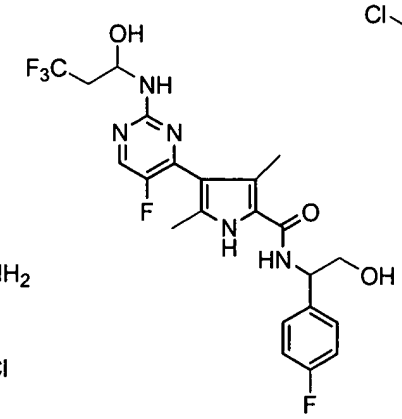

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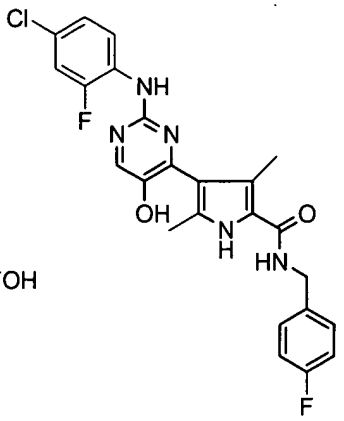

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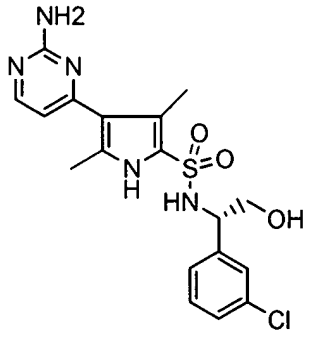

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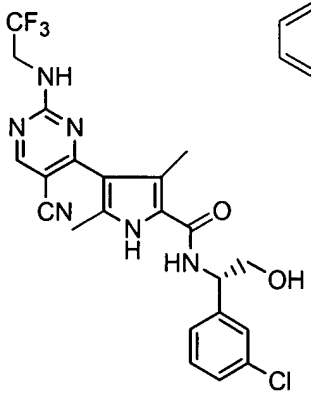

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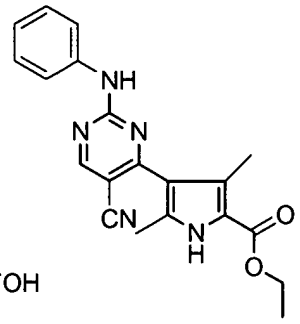

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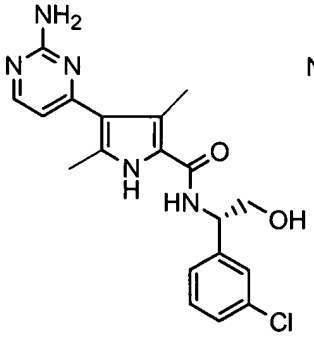

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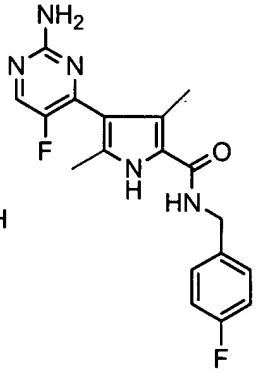

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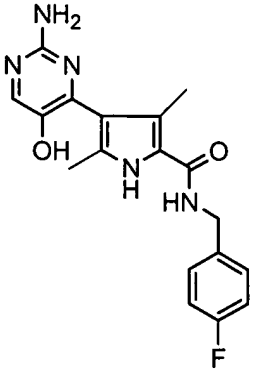

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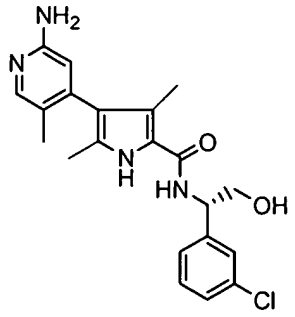

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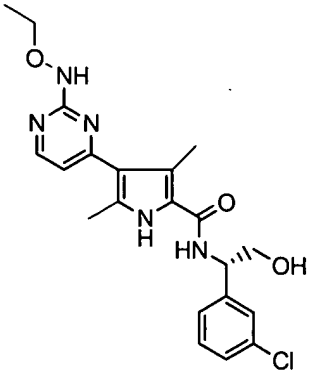

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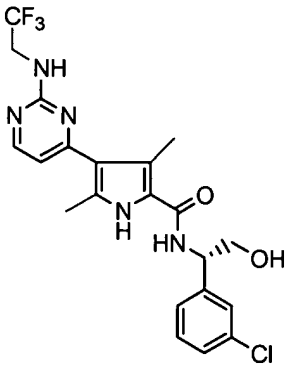

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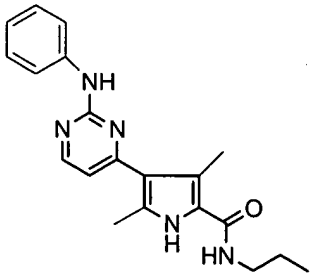

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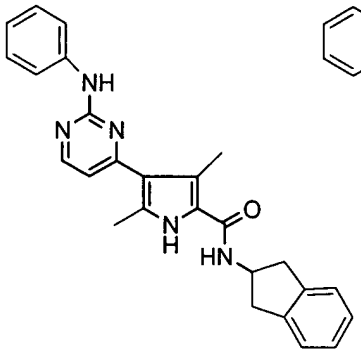

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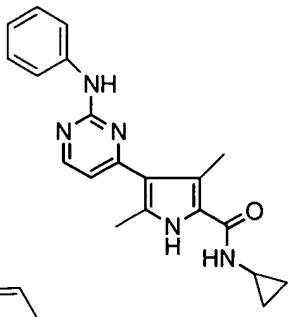

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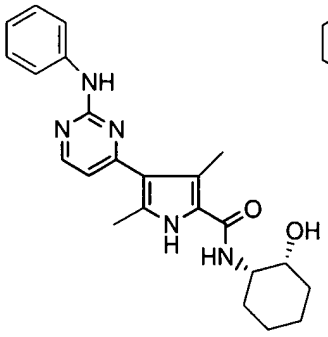

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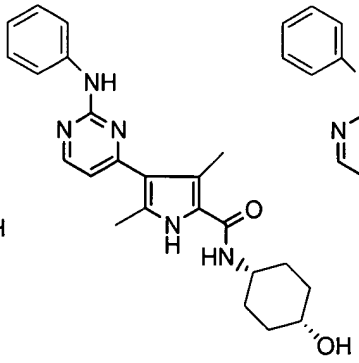

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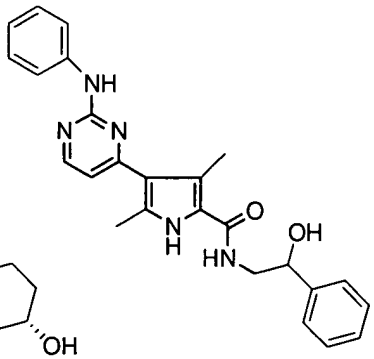

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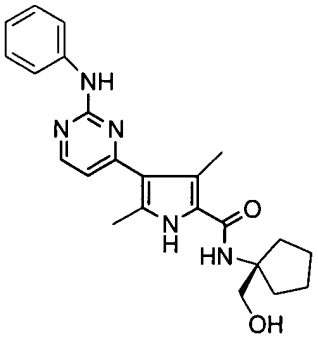

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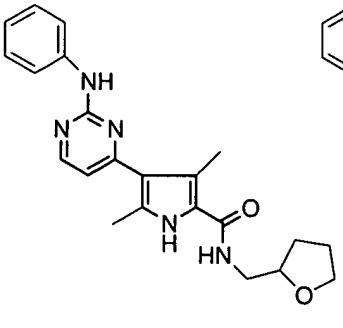

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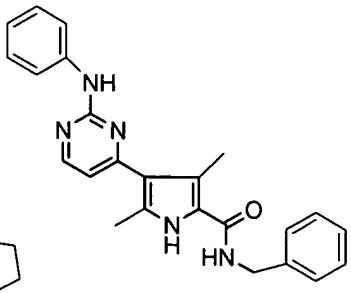

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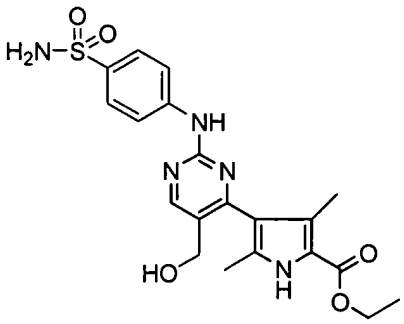

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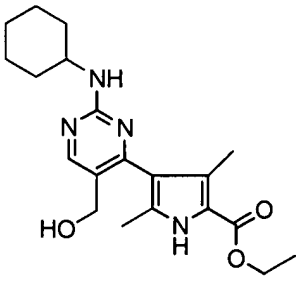

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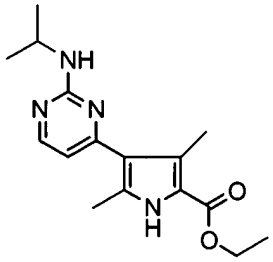

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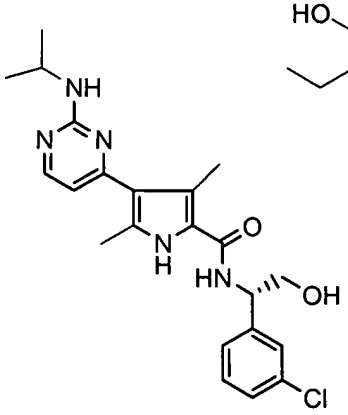

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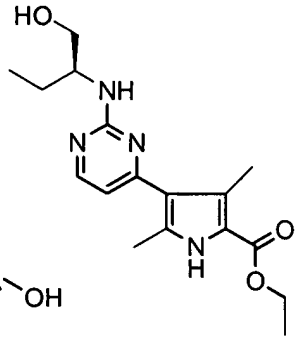

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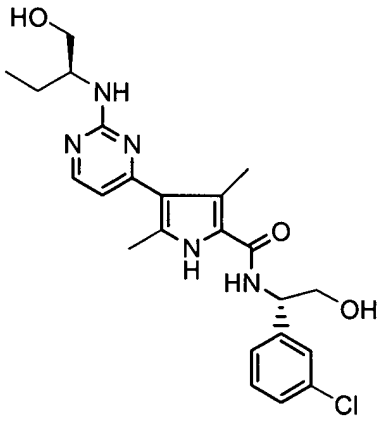

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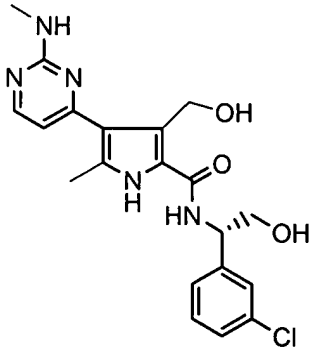

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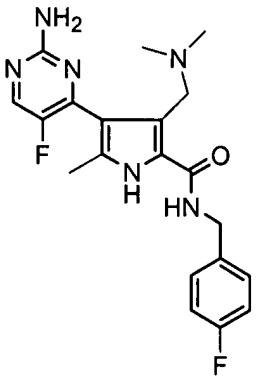

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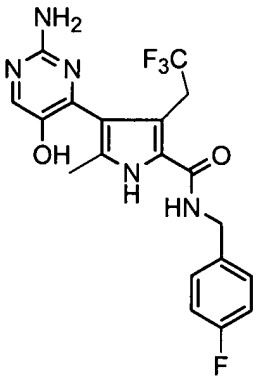

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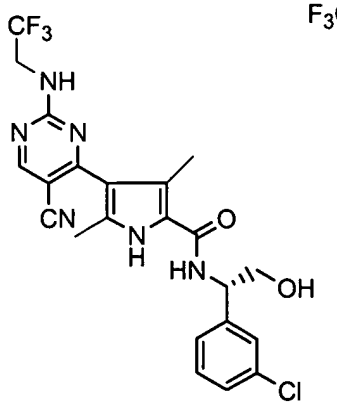

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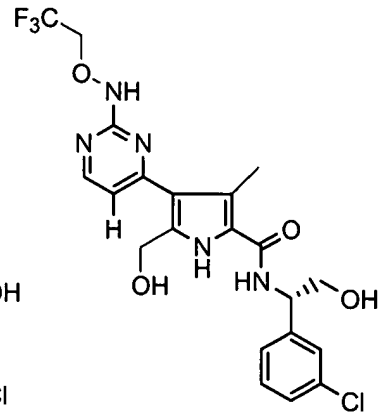

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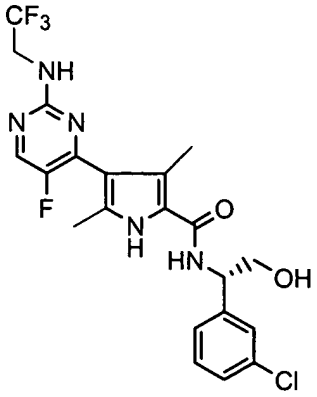

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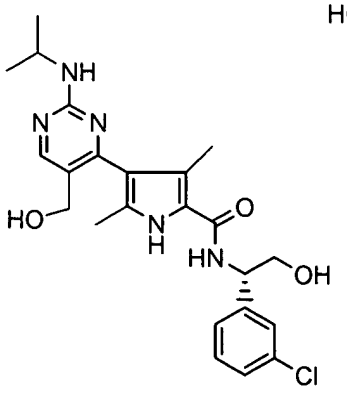

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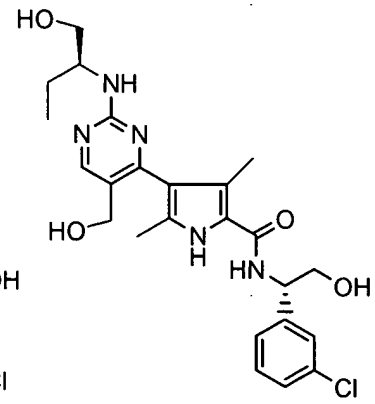

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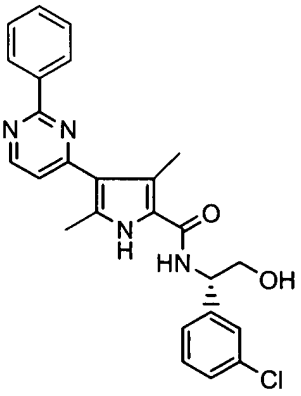

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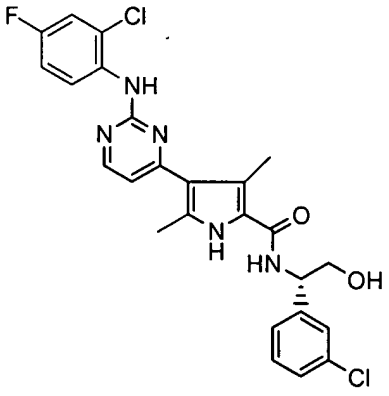

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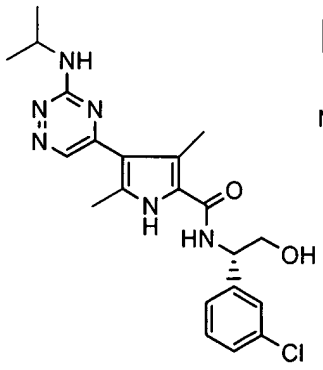

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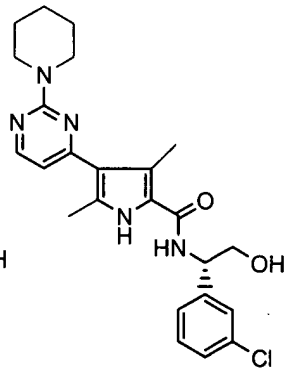

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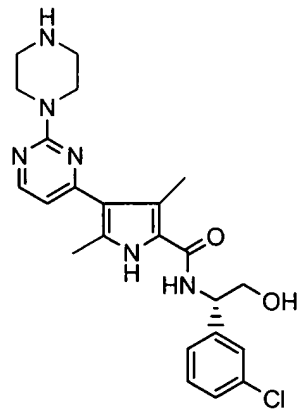

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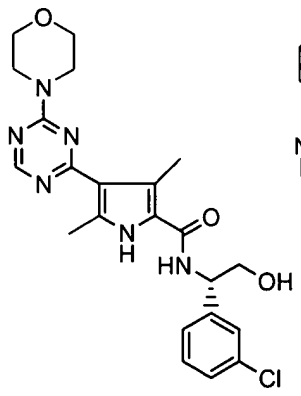

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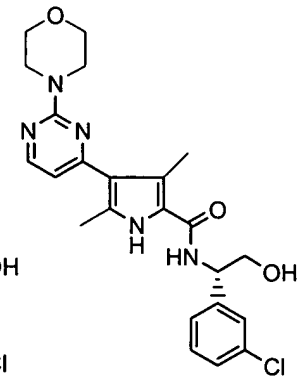

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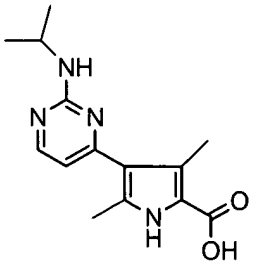

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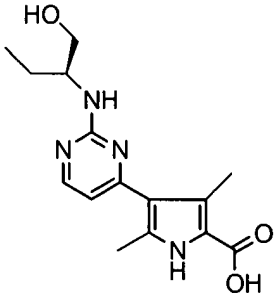

I-68.

12. A composition comprising an effective amount of a compound according to claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

13. The composition of claim 2, wherein the composition comprises said compound in an amount sufficient to measurably inhibit ERK2, JNK3, SRC, Aurora2, or GSK3 protein kinase activity.

14. The composition of claim 12, additionally comprising a therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, an agent for treating a neurological disorder, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, or an agent for treating immunodeficiency disorders.

15. A method of inhibiting ERK2, JNK3, SRC, Aurora2, or GSK3 protein kinase activity in a biological sample, which method comprises contacting said biological sample with:

a) a composition according to claim 12; or

b) a compound according to claim 1.

16. A method of inhibiting ERK2, JNK3, SRC, Aurora2, or GSK3 protein kinase activity in a patient, which method comprises administering to said patient:

a) a composition according to claim 12; or

b) a compound according to claim 1.

17. A method of treating or lessening the severity of a disease, condition or disorder, in a patient in need thereof, selected from a proliferative disorder, a cardiac disorder, a neurodegenerative disorder, an autoimmune disorder, a condition associated with organ transplant, an inflammatory disorder, an immunologically mediated disorder, or a bone disorder, comprising the step of administering to said patient:

a) a composition according to claim 12; or

b) a compound according to claim 1.

18. The method according to claim 17, comprising the additional step of administering to said patient an additional therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, or an agent for treating immunodeficiency disorders, wherein:

(a) said additional therapeutic agent is appropriate for the disease being treated; and

(b) said additional therapeutic agent is administered together with said composition as a single dosage form or separately from said composition as part of a multiple dosage form.

19. A method for treating or lessening the severity of a disease, disorder, or condition, in a patient in need thereof, selected from cancer, asthma, diabetes, stroke, schizophrenia, osteoperosis, rheumatoid arthritis, myocardial infarction, Alzheimer's disease, Parkinson's disease, Huntington's disease, or Amyotrophic Lateral Sclerosis, which method comprises administering to said patient a composition according to claim 12.

20. The method according to claim 19, wherein said disease, disorder, or condition is a cancer selected from breast, ovary, cervix, prostate, testis, genitourinary tract, esophagus, larynx, glioblastoma, neuroblastoma, stomach, skin, keratoacanthoma, lung, epidermoid carcinoma, large cell carcinoma, small cell carcinoma, lung adenocarcinoma, bone, colon, adenoma, pancreas, adenocarcinoma, thyroid, follicular carcinoma, undifferentiated carcinoma, papillary carcinoma, seminoma, melanoma, sarcoma, bladder carcinoma, liver carcinoma and biliary passages, kidney carcinoma, myeloid disorders, lymphoid disorders, Hodgkin's, hairy cells, buccal cavity and pharynx (oral), lip, tongue, mouth, pharynx, small intestine, colon-rectum, large intestine, rectum, brain and central nervous system, or leukemia.

21. The method according to claim 19, wherein said disease, disorder, or condition is melanoma or a cancer selected from breast, colon, or pancreatic.

22. The method according to claim 19, wherein said disease, disorder, or condition is melanoma, lymphoma, neuroblastoma, or leukemia, or a cancer selected from colon, breast, lung, kidney, ovary, pancreatic, renal, CNS, cervical, prostate, or cancer of the gastric tract.

23. The method according to claim 19, wherein said disease, disorder, or condition is stroke.

24. A method of treating or lessening the severity of hypercalcemia, osteoporosis, osteoarthritis, cancer, symptomatic treatment of bone metastasis, or Paget's disease in a patient in need thereof, comprising the step of administering to said patient:

a) a composition according to claim 12; or

b) a compound according to claim 1.

25. A method of enhancing glycogen synthesis in a patient in need thereof, comprising the step of administering to said patient:

a) a composition according to claim 12; or

b) a compound according to claim 1.

26. A method of inhibiting the production of hyperphosphorylated Tau protein in a patient in need thereof, comprising the step of administering to said patient:

a) a composition according to claim 12; or

b) a compound according to claim 1.

27. A method of inhibiting the phosphorylation of β-catenin in a patient in need thereof, comprising the step of administering to said patient:

a) a composition according to claim 12; or

b) a compound according to claim 1.

28. A method of decreasing sperm motility in a male patient, comprising the step of administering to said patient:

a) a composition according to claim 12; or

b) a compound according to claim 1.

29. A method of treating depression in a patient in need thereof, comprising the step of administering to said patient:

a) a composition according to claim 12; or

b) a compound according to claim 1.